The Activity of Some Herbs with or Without Honey in Protecting the Liver against Carbon Tetrachloride Hepatotoxicity in Female Albino Rats

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ABSTRACT

A total number of 50 Sprague Dawley strain female albino rats (200±10g each) were used in the present study, to evaluate the effect of phytogenic diet (*Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum*) at 9% levels on the body weight gain (BWG), liver enzymes activities (ALT and AST), serum protein fractions (TP, ALB, GLB and ALB/GLB ratio), lipids profile (TC, TG, VLDL-c, LDL-c and HDL-c) and AI. Rats divided into 10 groups (5 rats each) including control negative (–Ve) fed on basal diet only, control positive (+Ve) fed on basal diet and injected with CCl_4, as well as 4 groups consumed a diet containing 9% of herbs without honey and other 4 groups consumed their diets containing 4.5% of herbs powder plus 4.5% of honey. Microscopic evaluations of the liver revealed CCl_4-induced lesions and related toxic manifestations that were minimal in the liver of rats pretreated with powders at the dose of 9%/ kg of body weight. The results revealed that all herbs improved the tested parameters, especially that of the *Rheum* diet. In all diets treatments honey alleviated more the hepatopathy in CCl_4 injected rats.

Keywords: Hepatoprotective, *Gentiana*, *Glycyrrhizae*, *Ginseng*, *Rheum*, honey.

INTRODUCTION

The liver is a critical hub for numerous physiological processes. These include macronutrient metabolism, blood volume regulation, immune system support, endocrine control of growth signaling pathways, lipid and cholesterol homeostasis, and the breakdown of xenobiotic compounds, including many current drugs **(Gao *et al.*, 2021)**. Processing, partitioning, and metabolism of macronutrients provide the energy needed to drive the aforementioned processes and are therefore among the liver's most critical functions **(Haro *et al.*, 2019)**. Moreover, the liver's capacities to store glucose in the form of glycogen, with feeding, and assemble glucose via the gluconeogenic pathway, in response to fasting, are critical. The liver oxidizes lipids, but can also package excess lipid for secretion to and storage in other tissues, such as adipose. Finally, the liver is a major handler of protein and amino acid metabolism as it is responsible for the majority of proteins secreted in the blood, the processing of amino acids for energy, and disposal of nitrogenous waste from protein degradation in the form of urea metabolism **(Gao *et al.*, 2021)**. Liver disorders have been classified in the high-priority areas of health care. According to an estimate by the World Health Organization, approximately 500 million people of the world are suffering from a severe form of liver disorder, that is, chronic hepatitis **(Al-Asmari *et al.*, 2014)**.

Herbal products, a complementary and alternative therapy, are increasingly gaining popularity in daily life and health care all over the world **(AL-Rawi *et al.*, 2017)**. Herbal medicine is mainly applied in promoting health and the treatment of chronic diseases. It is also plays a crucial role in multi-component therapeutics **(Wu *et al.*, 2019)**. With the increasing usages of herbal medicine, the need for quality control has also increased. Currently, the regulations and pharmacovigilance about herbal medicines are still incomplete and need to be enhanced and improved **(Skalli and Jordan, 2017)**. Medicine of herbal origin may serve as a feasible therapy for the prevailing liver problems because of their safety, easier availability, cost-effectiveness, and environmental friendliness **(Ali *et al.*, 2018)**. Medicinal plants have acquired importance in the healthcare system throughout the world for their proven and effective therapeutic properties **(Anand *et al.*, 2019)**. An estimated 80% of the world's population is relying on **(Hosseinzadeh *et al.*, 2015)**.

Gentiana (*Gentiana rigescens*) is a precious and highly appreciated Chinese herbal medicine, which is widely distributed in the southwest of China, especially in Yunnan Province **(Wu *et al.*, 2017)**. As a perennial herb, the root and rhizome are used as the primary medicinal part. This medicine mainly contains iridoids, lignans, triterpenes and others **(VanWyk and Wink, 2018)**. Among them, gentiopicroside, which belongs to the iridoid class of compounds, is the main active constituents of *Gentiana* and it is recorded as a quality criterion **(Ding *et al.*, 2018)**. This compound has long been used in the treatment of hepatic diseases, as it has liver-protective and choleretic functions **(Wu *et al.*, 2017)**. Reports indicated that *Gentiana* was commonly used for clearing away damp-heat to cure jaundice, purging fire in the liver and gall bladder, exhibiting anti-inflammatory effects, and possessing antifungal activities against the plant pathogen *Glomerella cingulata*, etc. **(Mi *et al.*, 2019)**.

Glycyrrhizae (*Glycyrrhizae radix*) is the rhizome of *Glycyrrhizae inflate*; *Glycyrrhizae uralensis* or *Glycyrrhizae glabra*. They are widely distributed in the northwest and northeast of China **(Li *et al.*, 2020)**. The main saponin, glycyrrhizin, and its aglycone, glycyrrhetinic acid, have shown anti-inflammatory, anti-ulcer, hepatoprotective, immunomodulatory and antivirus activities; flavonoids, including flavanones such as liquiritin apioside, liquiritin and liquiritigenin, and chalcones, such as isoliquiritin apioside, isoliquiritin and isoliquiritigenin, etc., have shown antitussive, anti-inflammatory, anti-allergic and anti-tumor effects **(Cooper and Deakin, 2020)**; in addition, glycycoumarin, a species-specific compound to *Glycyrrhizae uralensis Fischer*, has antispasmodic and antibacterial activities **(Öztürk *et al.*, 2018)**.

Ginseng (*Ginseng radix*), the dried root and rhizome of *Panax ginseng* C.A. Meyer, is one of the most famous and valuable traditional Chinese herbs in Asia. In recent years, it has been widely used for making functional foods in many other countries like in Europe and in the USA **(Bigliardi and Galati, 2013)** and **(Shahrajabian *et al.*, 2020)**. The chemical composition of ginseng includes carbohydrates, nitrogen-containing compounds, fat-soluble substances, minerals, and ginseng saponin (ginsenoside), and the chemical structure of approximately 30 types of ginsenosides has been determined **(Hyun *et al.*, 2020)**. Ginseng saponin is present in the form of a glycoside, a combined aglycone and sugar hence, its name ginsenoside. Ginseng saponin is divided into a four-ring structure triterpenoid dammarane-type saponin, including protopanaxadiol- and protopanaxatriol-type saponins, and a five-ring structure oleanane-type saponin **(Piao *et al.*, 2020)**. As the major active component of Korean ginseng, ginsenoside has predominantly been used to establish the quality specifications of ginseng. Moreover, Korean ginseng contains various functional constituents in addition to saponin, such as phenolic compounds with antioxidant activity, polyacetylene, which exhibits cytotoxicity to cancer cells, sesquiterpene, an essential oil, and acidic polysaccharides, which are currently studied actively in relation to immune responses **(Mohsin *et al*., 2020)**.

Rheum (*Rheum palmatum*), commonly known as Chinese rhubarb, belongs to the family *Polygonaceae*. *Rheum* is rich in anthraquinones and tannins, and its extracts exhibit a wide array of pharmacological properties including laxative, hepato-protective, antiviral, antibacterial, antidiabetic and antimetastatic effects **(Pengelly and Bone, 2020)**. *Rheum* is a medicinal plant, which is a species of perennial, stout herbs that are distributed in the temperate and subtropical regions of the world, chiefly in Asian countries. *Rheum* is not planted or grown; it grows wildly **(Benjamin, 2018)**.

The aims of the present study were thus to present a comprehensive overview of the therapeutic potential properties of *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* with a view to their traditional and popular uses for protective or treatment of liver diseases, development of new drugs to treat various human diseases, return to nature by activating the use of remedies of natural origin instead of therapies of chemical origin, and spreading awareness and nutritional education of the benefits of medicinal plants and how to use them.

MATERIALS AND METHODS

Materials:

Basal diet was installed its ingredients from casein 10%, corn oil 10%, mineral's mixture 4%, vitamin's mixture 1%, fiber 4% and corn starch up to 100% according to **(Campbell, 1961)** and **(Reeves *et al*., 1993)**. The minerals mixture, which was used in this experiment as recommended by **(Hegsted *et al*., 1941)**. The vitamins mixture as recommended by **(Muller, 1964)** were purchased from El-Gomhorya Company for Trading Drugs, Chemicals and Medical Instruments, Tanta-Gharbia-Egypt. ***Note*** (12.3 g of casein gives 10.0 g protein; 1 IU equal 1.02 mg; 1 ppm = 0.0001%).

Gentiana, *Glycyrrhizae*, *Ginseng* and *Rheum* have been purchased from the local market and have been bought from grocers from Cairo governorate, Egypt. All herbs were cleaned thoroughly by washing, and cut into small slices and dried in a drying oven at temperature 50°C for 3 days, then crushed and milled as a fine powder.

Animals; fifty female albino rats, Sprague Dawley strain, weighing 200 ±10 g, were obtained from Serum and Vaccine Center-Cairo.

CCl_4 and chemical kits for biochemical analysis were obtained from El-Gomhorya Company for Trading Drugs, Chemicals and Medical Instruments, Cairo, Egypt as 10% liquid solution. It was dispensed in white plastic bottles each containing one liter as a toxic chemical material for liver poisoning according to Passmore and Eastwood **(Nicolle *et al.*, 1986)**. At the same time, it is mixed with paraffin oil which is obtained from the pharmacy for dilution during the induction.

Induction of liver intoxication in rats; forty-five (45) female albino rats were treated subcutaneous injection of carbon tetrachloride (CCl_4) in paraffin oil 50% V/V (2 ml/kg b. wt.) twice a week for two weeks to induce chronic damage of the liver according to the method described by **(Jayasekhar *et al.*, 1997)**. After the injection of CCl_4, blood samples were obtained by retro orbital method to ensure the occurrence of liver injury and to estimate liver function **(Somasundaram *et al.*, 2010)**.

Animals groups; fifty Sprague-Dawley female albino rats, each weighing 200±10 g, were housed in group cages under conditions and fed on a basal diet for adaptation for at least seven days before experiments. The rats were divided into (10) main groups (5 rats each) as follows:

- Group (1) negative or normal group fed on basal diet only.
- The other rats were injected by CCl_4 then divided into 9 groups as follows:
  - Group (2) positive group fed on basal diet.
  - Group (3) fed on basal diet plus 9% of *Gentiana*.
  - Group (4) fed on basal diet plus 9% of *Glycyrrhizae*.
  - Group (5) fed on basal diet plus 9% of *Ginseng*.
  - Group (6) fed on basal diet plus 9% of *Rheum*.
  - Group (7) fed on basal diet plus 9% of an equalized mixture of *Gentiana* and honey.
  - Group (8) fed on basal diet plus 9% of an equalized mixture of *Glycyrrhizae* and honey.

- Group (9) fed on basal diet plus 9% of an equalized mixture of *Ginseng* and honey.
- Group (10) fed on basal diet plus 9% of an equalized mixture of *Rheum* and honey.

Methods:

Biological evaluation; during the experimental period (28 days), body weight was recorded every week. Biological evaluations of the different diets were carried out by determination of body weight gain (BWG) according to **(Chapman *et al.*, 1959)**, using the following formulas: BWG (g) = Final weight - Initial weight

Biochemical analysis; blood samples were used for determination of the concentration following parameters by commercially available (BioMerieux) kits: determination of total protein (TP), albumin (ALB), globulin (GLB) and ALB/GLB ratio were carried out according to **(Nishi *et al.*, 1985)**; total cholesterol (TC) was measured according to **(Thomas, 1992)**, triglyceride (TG) was carried out according to **(Klotzsch and McNamara, 1990)**, high-density lipoprotein cholesterol (HDL-c) was carried out according to **(Lopes-Virella *et al.*, 1977)**, (low-density lipoprotein cholesterol (LDL-c) **=** TC – [HDL-c + VLDL-c]) was calculated according to **(Castelli *et al.*, 1977)**, (very low-density lipoprotein cholesterol (VLDL-c) = Triglycerides/5) was calculated according to **(Srivastava *et al.*, 2002)**; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were carried out according to **(Reitman and Frankel, 1957)**. Determination the atherogenic index (AI) = VLDL-c + LDL-c/HDL-c was carried out according to **(Tagoe *et al.*, 2020)** and **(Garg *et al.*, 2020)**.

Statistical analysis was performed by using the computer program statistical package for social science **SPSS, 1998** and compared with each other using the suitable tests. The mean±SD was indicated. A paired T. test was used to evaluate differences between the groups of rats and their respective control. For statistical analysis of time-course experiments, multiple measurements ANOVA were performed **(Rahman and Muktadir, 2021)**.

Histopathological examination; specimens from the halves of the liver were taken immediately after weighing the organ of the rats and immersed in 10% neutral buffered formalin. The fixed specimens were then trimmed, washed, and dehydrated in ascending grades of alcohol, then cleared in xylene, and stained with Hematoxylin and Eosin (H&E) and examined microscopically according to **(Bancroft and Gamble, 2008)** and **(Loha *et al.*, 2019)**.

RESULTS AN D DISCUSSION

Body weight gain:

Data presented in a table (1) show the body weight gain (BWG) of hepatopathy rats. Group 2 (Positive control) had a significant decrease in body weight gain when compared to the normal rats group 1 (Negative control) by 27.0 and 44.8 respectively. It is evident that due to CCl_4 injection hepatopathy lowered considerably the BWG resulting in a 65.9% increase for control (–Ve) rats compared to that of the control (+Ve) group. The obtained results in a table (1) are in the same trend of Shehata 2012, Riad 2014 and Elbanna 2014 who found that injected rats by CCl_4 caused a decrease in BWG **(Abd EL-Meged and Al-Shehri, 2020)** and this agrees with our results. From the results of a table (1), it could be noticed that BWG of hepatopathy rats improved with suggested diets with honey, provided that best effect recorded for *Gentiana* 4.5%, *Glycyrrhizae* 4.5%, *Ginseng* 4.5% or *Rheum* 4.5% equalized with honey 4.5%. Meanwhile, in this case difference for BWG of all diets with honey added at 4.5% of the basal diet (with 4.5% *Gentiana*, *Glycyrrhizae*, *Ginseng* or *Rheum*) showed a significance increase ($P\leq0.05$) in BWG when compared with the control positive group. This indicates the effective effect of honey in raising the efficiency of the active substances present in the herbs and thus relieving liver disease. Such improvement was so evident that any BWG level for diets with honey (49.0 - 52.4g) surpassed that of the control (-Ve) plain basal diet (44.8 g).

Table (1): Effect of phytogenic experimental diets on body weight gain of female albino rats

Groups and diets		BWG	
		g / 28 days	% of (+Ve)
Control	-Ve	44.8^{b}±4.33	65.9
	+Ve	27.0^{d}±3.94	-
Without honey	*Gentiana*	44.0^{c}±3.26	63.0
	Glycyrrhizae	44.0^{c}±3.58	63.0
	Ginseng	44.8^{b}±3.10	65.9
	Rheum	46.0^{b}±3.09	70.4
With honey	*Gentiana*	51.8^{a}±6.38	91.9
	Glycyrrhizae	49.0^{a}±2.58	83.0
	Ginseng	52.2^{a}±4.69	93.3
	Rheum	52.4^{a}±3.81	94.1

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at p≤0.05

Serum ALT and AST:

Data of table (2) show the effect of tested *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* diets without and with honey on activities of liver enzymes. It is obvious that AST and ALT activities rise due to hepatopathy and this may be due to damage of liver cells and escape of enzymes to the serum. This results were reported by **(Mohamed *et al.*, 2017)** where hepatopathy raised the AST activity to 116.8±3.37ul and ALT to 126.6±4.23ul of control (+Ve) group compared to control (-Ve) rats of 25.2±1.56 ul and 22.4±2.98 ul respectively. All phytogenic experimental diets improved levels of ALT and AST, while more improvement was recorded for phytogenic experimental diets with honey. Even for diets with honey showed the lowest improvement compared to the control (+Ve) group, being 69.2±2.76, 61.6±3.41, 63.4±3.26 and 48.4±2.71 for ALT; while, 89.6±3.31, 69.6±4.18, 72.6±3.83 and 63.6±3.61 for AST respectively were pronounced within 28 days. The reactive electrons species from CCl_4 induces rat liver cirrhosis that resembles the human disease, and it can serve as a suitable animal model for studying human liver cirrhosis **(Ahmed *et al.*, 2006)**. Toxicity experienced by the liver during CCl_4 poisoning results from the production of a metabolite;

CCl_4 which is a direct hepatotoxin responsible for change in cell permeability and it inhibits mitochondrial activity followed by cell death **(Ahmed *et al.*, 2009)**. It has also been reported that chronic CCl_4 exposure produced cirrhosis in rats **(Chieli and Malvadi, 2008)**. On the other hand, the study demonstrated that the treatment with *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* caused marked ameliorations of transaminase enzymes activity (ALT and AST). From the results of table (2), the best treatment was that of the *Rheum* with honey considering ALT and AST parameters. Honey showed more improvement for all diets.

Table (2): Effect of phytogenic experimental diets on ALT and AST of female albino rats

Groups and diets		AST		ALT	
		U/L	% of (+Ve)	U/L	% of (+Ve)
Control	-Ve	$25.2^{e}\pm1.56$	78.43	$22.4^{g}\pm2.98$	82.31
	+Ve	$116.8^{a}\pm3.37$	-	$126.6^{a}\pm4.23$	-
Without honey	*Gentiana*	$88.6^{b}\pm2.16$	24.14	$79.8^{bc}\pm4.05$	63.03
	Glycyrrhizae	$72.2^{d}\pm3.57$	38.19	$77.6^{bcd}\pm2.77$	38.71
	Ginseng	$73.6^{cd}\pm2.48$	36.99	$72.0^{bcde}\pm3.77$	43.13
	Rheum	$83.0^{bc}\pm3.26$	28.94	$81.4^{b}\pm3.33$	35.7
With honey	*Gentiana*	$89.6^{b}\pm3.31$	23.29	$69.2^{cde}\pm2.76$	45.34
	Glycyrrhizae	$69.6^{d}\pm4.18$	40.41	$61.6^{e}\pm3.41$	51.34
	Ginseng	$72.6^{cd}\pm3.83$	37.84	$63.4^{e}\pm3.26$	49.92
	Rheum	$63.6^{d}\pm3.61$	45.55	$48.4^{l}\pm2.71$	61.77

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at $p\leq0.05$

Serum protein fractions:

The results of a table (3) showed the serum protein fractions of hepatopathy rats as affected by feeding on phytogenic diets with and without honey. It could be noticed that TP, ALB, GLB and ALB/GLB ratio. Control (-Ve) rats revealed a percent increase of 64.25, 361.4, 824.3% and 49.67% decrease above parameters due to hepatopathy respectively. According to **(Marin *et al.*, 2013)** and **(AL-Shannaq and Yu, 2017)** who were reported the reduced hepatic synthesis of transport proteins may result in low serum albumin in patients with liver disease, possibly with the rise of serum globulin. **(Alade *et al.*, 2020)**; **(Kilany *et al.*, 2020)** and **(Bermúdez *et al.*, 2020)** were described that serum globulin concentration is sometimes used as a crude measure of the severity of the liver diseases. **(Mohamed, 2010)** showed that alternation of ALB/GLB ratio may occur due to the reduction in albumin and the elevation of globulin in serum, especially in some cases of biliary cirrhosis. This was found in the present work when hepatopathy rats were fed of *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* diets; the best diet for TP was that of all diets without honey and *Gentiana rigescens* of diets with a honey table (3). From the results of a table (3) for Alb *Rheum* with a honey diet point to a nonsignificance difference in serum compared to healthy rats, while at the same time reduced markedly compared to (-Ve), while for Glb all diets without honey except *Gentiana* showing very high significance but *Gentiana* revealed high significance, on the other hand *Gentiana* with honey point to very high significance, whereas *Glycyrrhizae* and *Ginseng* showed high significance. Finally for Alb/Glb ratio all diets without or with honey showed high significance except *Gentiana* without honey explain to be very highly significance compared to the (-Ve) group. The differences between the effects of a diets may be attributed to different levels of understanding with the potential health benefits as antioxidants **(Coats and Martirosyan, 2015)**.

Table (3): Effect of phytogenic experimental diets on serum protein fractions of female albino rats

Groups and diets		TP		ALB	
		g/dl	% of (+Ve)	g/dl	% of (+Ve)
Control	**-Ve**	6.8[a]±0.23	64.25	5.26[a]±0.32	361.4
	+Ve	4.14[b]±0.34	-	1.14[c]±0.31	-
Without honey	***Gentiana***	6.24[a]±0.41	50.73	3.38[b]±0.37	196.5
	Glycyrrhizae	6.6[a]±0.34	59.42	3.82[b]±0.44	235.1
	Ginseng	6.44[a]±0.45	55.56	3.74[b]±0.42	228.1
	Rheum	6.9[a]±0.24	66.67	4.2[b]±0.43	248. 4
With honey	***Gentiana***	6.72[a]±0.52	62.32	4.16[b]±0.35	264. 9
	Glycyrrhizae	6.59[d]±0.46	59.18	3.99[b]±0.4	250.0
	Ginseng	6.64[cd]±0.14	60.39	4.0[b]±0.42	250.9
	Rheum	7.3[d]±3.61	76.33	5.12[d]±0.5	349.1

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at p≤0.05

Table (3) continue: Effect of phytogenic experimental diets on serum protein fractions of female albino rats

Groups and diets		GLB		ALB/GLB ratio	
		g/dl	% of (+Ve)	Ratio	% of (+Ve)
Control	-Ve	$1.54^{b}±0.32$	49.67	$3.42^{a}±0.34$	824.3
	+Ve	$3.06^{a}±0.31$	-	$0.37^{d}±0.12$	-
Without honey	*Gentiana*	$2.86^{b}±0.61$	6.54	$1.18^{c}±0.65$	218.9
	Glycyrrhizae	$2.78^{c}±0.25$	9.15	$1.37^{b}±0.24$	270.3
	Ginseng	$2.70^{c}±0.55$	11.77	$1.39^{b}±0.87$	275.7
	Rheum	$2.7^{c}±0.38$	11.77	$1.56^{b}±0.46$	321.6
With honey	*Gentiana*	$2.56^{c}±0.64$	16. 34	$1.63^{b}±0.33$	340. 5
	Glycyrrhizae	$2.6^{b}±0.72$	15.03	$1.54^{b}±0.38$	316.2
	Ginseng	$2.54^{b}±0.47$	16.99	$1.58^{b}±0.4$	327.0
	Rheum	$2.18^{e}±0.2$	28.76	$2.35^{b}±0.2$	535.1

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at p≤0.05

Lipids profile:

The results of a table (4) showed the lipids profile of hepatopathy rats as influenced by feeding on phytogenic diets without or with honey. It was found that hepatopathy changed appreciably the lipids profile of rats leading to decreases in TC, TG, VLDL-c and LDL-c except HDL-c was increased; percent change of control (-Ve) compared to control (+Ve) were 46.06, 39.55, 39.55, 64.3 and 41.06% respectively. Similar trends of changes were found by **(Ragab *et al.*, 2019)** due to hepatopathy by CCl_4 injection. Meanwhile, for groups fed on herbs without honey observed that for total cholesterol the rats fed on *Ginseng* showed high significance, for triglycerides the group fed on *Rheum* pointed to high significance also that happened to VLDL-c, when for LDL-c all groups revealed to highly significance. But as for groups fed on herbs with a honey table (4) showed that for (TC) rats fed on *Gentiana* and *Glycyrrhizae* point to high significance, when TG the group fed on *Ginseng* revealed to very high significance, while for HDL-c the group fed on *Gentiana* and *Rheum* showed a significance. By feeding for 28 days on diets containing *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* diets TC, TG, VLDL-c and LDL-c were decreased, while HDL-c increased indicting healing of liver cells damaged by the disease. This may possibly be due to the antioxidation effect of phenolic compounds in the plant. **Chou *et al.*, 2008** investigated feeding the micronized insoluble fibers; significantly (P≤0.05) improved their abilities in lowering the concentrations of serum triglyceride, serum total cholesterol, and liver lipids to different extents by means of enhancing (P≤0.05) the excretion of lipids, cholesterol, and bile acids in feces. In the present work table (4) improvement of the lipids profile was much more pronounced considering *Ginseng* and *Rheum* diets without honey where compared with the healthy control (-Ve) group rats. Moreover, the addition of honey improved the action of used herbs.

Table (4): Effect of phytogenic experimental diets on serum lipids profile of female albino rats

Groups and diets		TC		TG	
		Mean±SD (mg/dl)	% change of (+Ve)	Mean±SD (mg/dl)	% change of (+Ve)
Control	-Ve	$116.4^{g}\pm4.3$	46.06	$92.0^{e}\pm3.2$	39.55
	+Ve	$215.8^{a}\pm5.7$	-	$152.2^{a}\pm9.0$	-
Without honey	*Gentiana*	$166.6^{cd}\pm4.0$	22.8	$112.0^{cd}\pm3.3$	26.41
	Glycyrrhizae	$162.6^{de}\pm3.5$	24.65	$98.4^{de}\pm5.7$	35.35
	Ginseng	$185.4^{b}\pm4.1$	14.09	$127.4^{cde}\pm5.8$	16.29
	Rheum	$177.0^{f}\pm3.8$	17.98	$131.8^{b}\pm3.\ 4$	13.4
With honey	*Gentiana*	$135.0^{b}\pm4.74$	37.44	$82.2^{e}\pm3.4$	45.99
	Glycyrrhizae	$132.5^{b}\pm3.6$	38.74	$90.4^{cde}\pm6.2$	40.61
	Ginseng	$122.6^{bg}\pm3.9$	43.19	$116.2^{c}\pm4.4$	23.65
	Rheum	$113.2^{g}\pm4.7$	47.54	$111.8^{d}\pm7.4$	26.54

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at p≤0.05

Table (4) continue: Effect of phytogenic experimental diets on serum lipids profile of female albino rats

Groups and diets		VLDL-c Mean±SD (mg/dl)	VLDL-c % change of (+Ve)	HDL-c Mean ± SD (mg/dl)	HDL-c % change of (+Ve)	LDL-c Mean ± SD (mg/dl)	LDL-c % change of (+Ve)
Control	-Ve	18.4^{bcd}±0.6	39.55	42.6^{a}±2.3	41.06	55.4^{bcd}±2.7	64.3
	+Ve	30.44^{a}±2.8	-	30.2^{b}±2.4	-	155.16^{a}±2.1	-
Without honey	*Gentiana*	24.4^{bc}±1.1	26.41	34.2^{ab}±2.3	13.25	110.0^{b}±4.5	29.11
	Glycyrrhizae	19.68^{bcd}±1.3	35.35	33.8^{ab}±2.6	11.92	109.12^{b}±3.6	29.67
	Ginseng	25.48^{b}±1.2	16.29	35.0^{ab}±3.2	15.89	124.92^{b}±2.7	19.49
	Rheum	26.36^{b}±0.7	13.4	37.6^{ab}±3.3	24.5	113.04^{b}±4.1	27.15
With honey	*Gentiana*	16.44^{bcd}±0.15	45.99	41.0^{a}±3.3	35.8	77.56^{bc}±4.35	50.01
	Glycyrrhizae	18.0^{bcd}±1.2	40.87	39.4^{ab}±3.4	30.41	74.8^{bc}±3.7	51.79
	Ginseng	23.24^{d}±0.9	23.65	37.8^{ab}±3.5	25.17	61.56^{bcd}±2.3	60.33
	Rheum	22.36^{bc}±1.5	26.54	42.0^{a}±3.0	39.07	48.84^{bcd}±4.8	68.52

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at $p\leq0.05$

Atherogenic index:

The results from the table (5) explain the atherogenic index of hepatopathy rats as influenced by feeding on phytogenic diets without or with honey. Atherogenic index was calculated as VLDL-c + LDL-c/HDL-c. The results from the table showed that all groups were fed on phytogenic diets without or with honey decreased when compared with the control (+Ve). As well as groups fed on herbs without honey revealed high significance when compared with the healthy control (-Ve) group rats.

Table (5): Effect of phytogenic experimental diets on serum atherogenic index of female albino rats

Groups and diets		AI	
		Mean±SD (mg/dl)	% change of (+Ve)
Control	-Ve	1.73^{bcd}±0.05	71.87
	+Ve	6.15^{a}±0.03	-
Without honey	*Gentiana*	3.87^{b}±0.65	37.07
	Glycyrrhizae	3.81^{b}±0.8	38.05
	Ginseng	4.3^{b}±0.75	30.08
	Rheum	3.71^{b}±0.8	39.68
With honey	*Gentiana*	2.29^{bc}±0.12	62.76
	Glycyrrhizae	2.36^{bc}±0.2	61.63
	Ginseng	2.24^{bc}±0.19	63.58
	Rheum	1.7^{bcd}±0.1	72.36

Each value represents mean± SD. Means with different superscript letters in the same column were significantly different at p≤0.05

Histopathological examination of liver:

Histopathologically, the liver of rats from the group (-Ve) showed the normal histological structure of the hepatic lobule **(Photos: A & B)**. However, examined sections from the group (+Ve) showed fibrosis of the hepatic capsule and cytoplasmic vacuolation of hepatocytes **(Photo: C)**, fibroplasia in the portal triad, portal infiltration with inflammatory cells **(Photos: D & A1)**, strands of fibroblasts between the hepatocytes and apoptosis of hepatocytes **(Photo: B1)**. While, the liver of rats from group (1) revealed Kupffer cells activation **(Photo: C1)**, fibrosis in the portal triad and appearance of newly formed bile ductules **(Photo: D1)**. The liver of rats from group (2) showed a fatty change of hepatocytes **(Photo: A11)** and Ballooning degeneration of hepatocytes **(Photo: B11)**. Examined sections from group (3) showed fibrosis of the hepatic capsule **(Photo: C11)**, apoptosis of hepatocytes and sinusoidal leukocytosis **(Photo: D11)**. Moreover, the liver of rats from group (4) revealed portal infiltration with inflammatory cells **(Photo: a)**, congestion of hepatic sinusoids and sinusoidal leukocytosis **(Photo: b)**. However, the liver of rats from group (5) revealed no changes except Kupffer cells activation **(Photo: c)**. However, the liver of rats from group (6) showed fibrosis of the hepatic capsule **(Photo: d)** and sinusoidal leukocytosis **(Photo: a1)**. Examined sections from group (7) revealed mild changes as congestion of the central veins **(Photo: b1)** and Kupffer cells activation **(Photo: c1)**. Moreover, the liver of rats from group (8) showed no changes except Kupffer cells activation **(Photos: d1 & a11)**. The liver from group (9) showed a fatty change of hepatocytes and congestion of hepatic sinusoids **(Photos: b11 & c11)**. However, sections from group (10) showed congestion of the central vein and hepatic sinusoids **(Photo: d11)**.

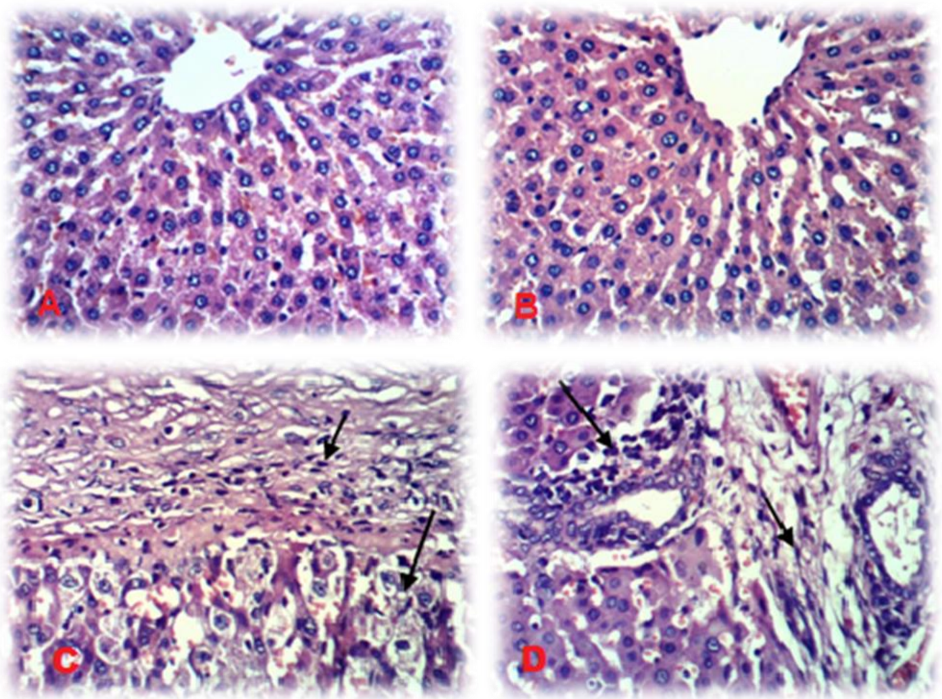


Photo (A): Liver of rat from group (-Ve) showing the normal histological structure of hepatic lobule (H & E X 400)
Photo (B): Liver of rat from group (-Ve) showing the normal histological structure of hepatic lobule (H & E X 400)
Photo (C): Liver of rat from group (+Ve) showing fibrosis of the hepatic capsule and cytoplasmic vacuolation of hepatocytes (H & E X 400)
Photo (D): Liver of rat from group (+Ve) showing fibroplasia in the portal triad and portal infiltration with inflammatory cells (H & E X 400)

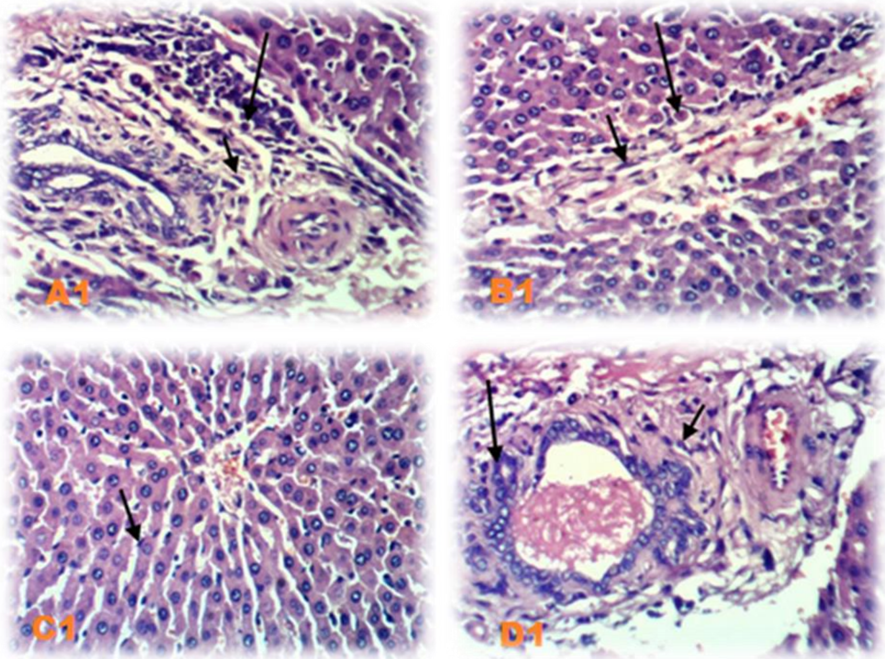
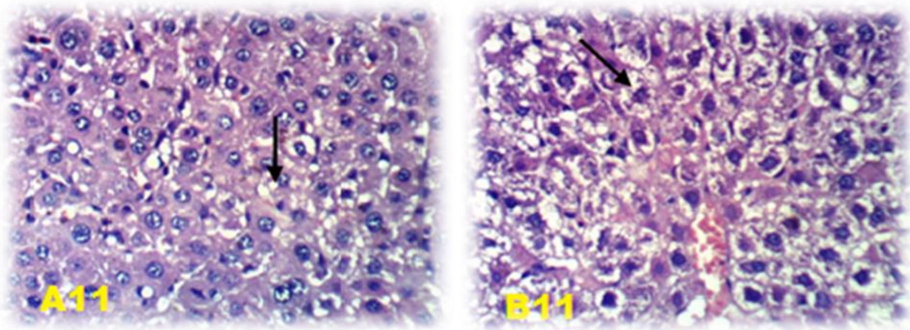


Photo (A1): Liver of rat from group (+Ve) showing fibroplasia in the portal triad and portal infiltration with inflammatory cells (H & E X 400)
Photo (B1): Liver of rat from group (+Ve) showing strands of fibroblasts between the hepatocytes and apoptosis of hepatocytes (H & E X 400)
Photo (C1): Liver of rat from group (1) showing Kupffer cells activation (H & E X 400)
Photo (D1): Liver of rat from group (1) showing fibrosis in the portal triad and appearance of newly formed bile ductules (H & E X 400)



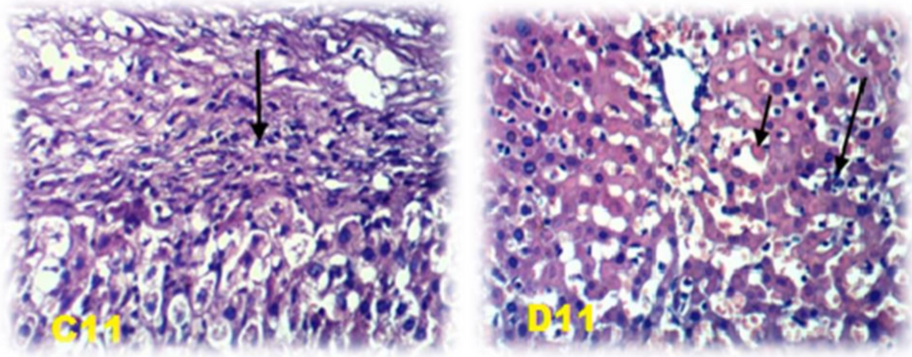


Photo (A11): Liver of rat from group (2) showing fatty change of hepatocytes (H & E X 400)
Photo (B11): Liver of rat from group (2) showing ballooning degeneration of hepatocytes (H & E X 400)
Photo (C11): Liver of rat from group (3) showing fibrosis of the hepatic capsule (H & E X 400)
Photo (D11): Liver of rat from group (3) showing apoptosis of hepatocytes and sinusoidal leukocytosis (H&E X 400)

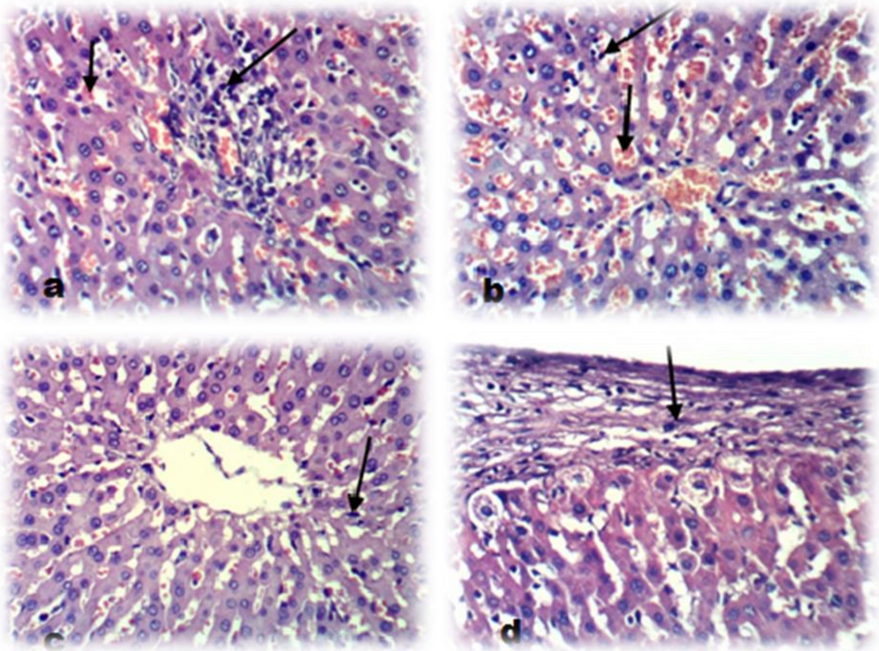


Photo (a): Liver of rat from group (4) showing congestion of hepatic sinusoids and portal infiltration with inflammatory cells (H & E X 400)
Photo (b): Liver of rat from group (4) showing congestion of hepatic sinusoids and sinusoidal leukocytosis (H & E X 400)
Photo (c): Liver of rat from group (5) showing Kupffer cells activation (H & E X 400)
Photo (d): Liver of rat from group (6) showing fibrosis of the hepatic capsule (H & E X 400)

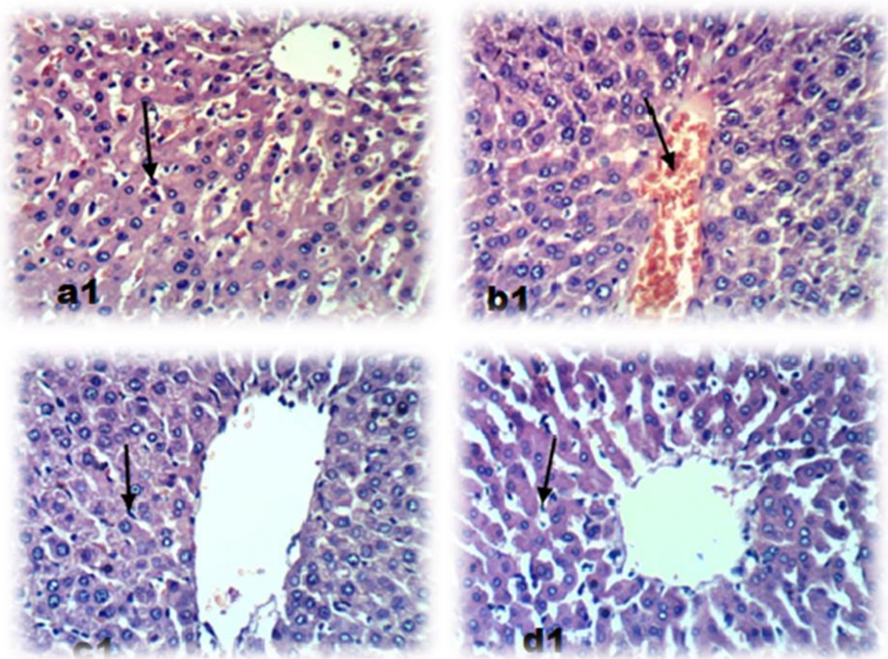


Photo (a1): Liver of rat from group (6) showing sinusoidal leucocytosis (H & E X 400)
Photo (b1): Liver of rat from group (7) showing congestion of central vein (H & E X 400)
Photo (c1): Liver of rat from group (7) showing Kupffer cells activation (H & E X 400)
Photo (d1): Liver of rat from group (8) showing Kupffer cells activation (H & E X 400)

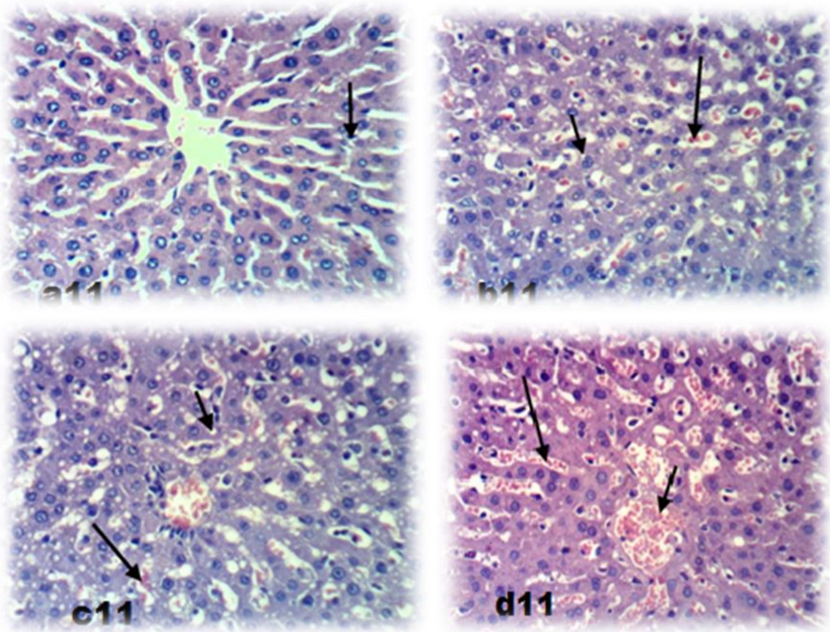


Photo (a11): Liver of rat from group (8) showing Kupffer cells activation (H & E X 400)
Photo (b11): Liver of rat from group (9) showing fatty change of hepatocytes and congestion of hepatic sinusoids (H & E X 400)
Photo (c11): Liver of rat from group (9) showing fatty change of hepatocytes and congestion of hepatic sinusoids (H & E X 400)
Photo (d11): Liver of rat from group (10) showing congestion of central vein and hepatic sinusoids (H & E X 400)

CONCLUSION

The present study concluded that feeding on diets containing *Gentiana*, *Glycyrrhizae*, *Ginseng* and *Rheum* improved the biological and biochemical parameters of the liver disorders rats, provided that the best results were obtained from the diet mix with honey. These effects are associated with amelioration of degenerative histopathological changes in liver tissue induced by CCl_4.

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مستخلص عربى

نشاط بعض الأعشاب مع أو بدون العسل فى حماية الكبد ضد تسمم الكبد برابع كلوريد الكربون فى إناث الفئران البيضاء

ساره محمود مصطفى عمر

مدرس بقسم التغذية وعلوم الأطعمة

جامعة الأزهر – طنطا – مصر

نبذة مختصرة

تم استخدام مجموعة مكونة من 50 فأر أنثى من سلالات Sprague Dawley البيضاء (200±10 جم لكل منهم) في هذه الدراسة، لتقييم تأثير التوليفات الغذائية النباتية (الجينتيانا وجذور الجليسيرزيزا وجذور الجينسينج والراوند) في مستويات 9٪ على زيادة وزن الجسم (BWG) وإنزيمات الكبد (ALT وAST) وبروتينات المصل (TP وALB وGLB ونسبة ALB/GLB) ودلائل الدهون (TC وTG وVLDL-c وLDL-c وHDL-c) ومؤشر تصلب الشرايين (AI). الفئران قسمت إلى 10 مجموعة (5 فئران فى كل مجموعة) المجموعة الضابطة السالبة (-Ve) التى تغذت على النظام الغذائي الأساسى فقط، والمجموعة الضابطة الموجبة (+Ve) التى تغذت على النظام الغذائي الأساسى وتم حقنها ب CCl_4، وكذلك 4 مجموعات تغذت على توليفة غذائية تحتوي على 9٪ من الأعشاب دون تناول العسل و 4 مجموعات أخرى احتوت توليفاتهم الغذائية على 4.5٪ من مسحوق الأعشاب بالإضافة إلى 4.5٪ من العسل. وكشفت النتائج أن جميع الأعشاب المختبرة حسنت المعاملات المختبرة، خاصة تلك التى تحتوى فى توليفتها الغذائية على الراوند. وفي جميع علاجات التوليفات الغذائية، خفف العسل كثيراً من اعتلال الكبد في الفئران المصابة بـ CCl_4. ودل ذلك على وجود بنية طبيعية لقطاع من الكبد كما هو الحال في المجموعة الضابطة السالبة.

الخلاصة: خلصت الدراسة الحالية إلى أن التغذية على التوليفات المحتوية على الجينتيانا وجذور الجليسيرزيزا وجذور الجينسينج والراوند والعسل أدت إلى تحسين المعايير البيولوجية والكيميائية الحيوية للفئران المصابة باختلال فى وظائف الكبد،

شريطة أن أفضل النتائج التي تم الحصول عليها من مزيج التوليفة الغذائية مع العسل. وترتبط هذه التأثيرات بتحسين التغيرات النسيجية المرضية في أنسجة الكبد التي يسببها رابع كلوريد الكربون.

الكلمات المفتاحية: الأنشطة الوقائية للكبد، الجينتبانا، جذور الجليسيرزيزا، جذور الجينسينج، الراوند، العسل.